

Applicants: Taka Aki Sato and Junn Yanagisawa
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REMARKS

Claims 121-141 are pending and under examination in the subject application. No claim has been added, canceled, or amended herein. Accordingly, claims 121-141 are still pending and under examination.

In view of the remarks below, applicants maintain that the Examiner's rejections have been overcome, and respectfully request that they be withdrawn.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 121-141 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner states that the phrase "consisting essentially of" recited in claims 121 and 139, is used in situations where it is clear that addition of other elements may not significantly alter a claimed composition. Specifically, the Examiner alleges that in the case of peptides, it is not clear how a peptide may have additional amino acids added that would significantly alter the structure of the peptide.

In response, applicants respectfully traverse the Examiner's rejection. Applicants contend that the language in claims 121 and 139 particularly points out and distinctly claims the subject invention. The phrase "consisting essentially of" has a well-established meaning. According to M.P.E.P. §2111.03, the transitional phrase "consisting essentially of" limits the

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scope of a claim to the specified materials or steps and those that do "not materially affect the basic and novel characteristic(s)" of the claimed invention (emphasis added). *In re Hertz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976).

In addition, in *Ex Parte Hoffman*, 12 USPQ2d 1061, 1063-64, as discussed in M.P.E.P. §2111.03, the Board of Patent Appeals and Interferences stated that "consisting essentially of" is typically used and defined in the context of compositions of matter. Therefore, the use of the transitional phrase "consisting essentially of" is proper to describe a peptide, which is a composition of matter. Furthermore, it is well known to a person skilled in the art that the addition of amino acids to a peptide is possible without altering its properties. Hence, applicants maintain that the rejected claims are well defined and particularly point out the subject matter which applicants regard as the invention.

In view of these remarks, applicants maintain that claims 121-141 satisfy the requirements of 35 U.S.C. §112, second paragraph.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 121-141 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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In response, applicants respectfully traverse the Examiner's rejection.

The test for enablement is whether one skilled in the art could, at the time of the invention, make and use the claimed invention based on the disclosure and the information known in the art without undue experimentation. Applicants maintain that the claimed invention satisfies the test for enablement, and that the Examiner has not set forth sufficient grounds for concluding otherwise.

The subject invention comprises a method for identifying compounds that inhibit the binding of a signal transducing protein with a cytoplasmic protein. This invention is based, at least in part, on applicants' surprising discovery of the new consensus sequence (S/T)-X-(V/I/L) composed of only three amino acids found in the carboxyl-terminus of signal transducing proteins that bind to PDZ domains of cytoplasmic proteins. Accordingly, the invention may be practiced using a signal transducing protein that contains the consensus sequence to find compounds that will alter the binding of the carboxyl terminus domain, thereby providing a compound that either inhibits or induces the respective signaling pathway.

In support of the rejection, the Examiner alleges that the specification does not reasonably enable the claimed methods because it allegedly fails to teach the biological significance of any combination of signal transducing proteins and cytoplasmic proteins other than that of Fas and FAP1. Therefore, the Examiner concludes that given the breadth of the claims with respect to the scope of the disclosure of the specification and what is known in the prior art, one skilled

in the art would be forced to engage in undue experimentation in order to make or use the subject invention.

Applicants disagree with the Examiner's position. First, applicants maintain that the specification as filed teaches each and every step of the claimed methods. Such teaching can be found in the specification, *inter alia*, at page 3, lines 16-24, listing proteins that interact with PDZ domains and their associated cytoplasmic proteins; *inter alia*, at page 12, line 31 to page 13, line 12, and, *inter alia*, at page 15, line 26 to page 16, line 9, detailing methods of use; *inter alia*, at page 14, lines 7-12, and at page 17, lines 12-17, providing examples of the methods; *inter alia*, at page 15, lines 1-3 and 12-14, and Figures 7A, 7B, 7C, 7F, and 7G, defining the signal transducing proteins, providing examples, and sequences; *inter alia*, at page 28, line 6 to page 30, line 37, and Figures 3B, 3C, 4B, and 4D, detailing the experimental results. Hence, applicants maintain that the above teachings in the specification, coupled with the pertinent teachings of the prior art, would clearly enable one skilled in the art to practice the claimed methods.

Second, applicants maintain that the biological significance of combinations in addition to Fas/FAP1 need not be known in order for the enablement requirement to be satisfied. All that is required by the rejected claims is that binding between two specific types of proteins be measured under specified circumstances.

Nevertheless, as detailed below by way of example, the prior art discloses NMDA receptors, K⁺ Channels, CD4 receptors, serotonin receptors, and p75 receptors and the cytoplasmic

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proteins with which these receptors are associated, and the function of such association.

The NMDA receptor, which has a central role in synaptic plasticity and memory formation, is associated with the Postsynaptic Density Protein PSD-95, whose second PDZ domain binds at the carboxyl terminus of NMDA to regulate the assembly of multi-protein complexes involved in NMDA receptor-mediated synaptic plasticity. (Kornau et al., submitted as Exhibit I in an April 12, 1999 Communication)

K⁺ Channels bind with PSD-95 at its carboxyl terminus to mediate the cell-surface clustering critical for neuronal signaling. (Kim et al., submitted as Exhibit H in an April 12, 1999 Communication)

The p75 receptor is associated with the Nerve Growth Factor NGF and enhances cell survival when bound, while inducing apoptosis when unbound (Rabizadeth, et al. (1993), and Rabizadeth, et al. (1994), submitted as Exhibits A and B, respectively, in the April 30, 2002 Communication). Furthermore, as reported in the subject specification, *inter alia* on page 32, lines 3-30, the p75 receptor interacts with FAP1 at its carboxyl terminus, and plays a role in the apoptotic signal transduction in neuronal cells.

These prior art teachings exemplify the many known protein combinations for which the instant methods are applicable. Applicants maintain that the above teachings of the prior art, coupled with the specification, would clearly enable one skilled in the art to practice the claimed methods.

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The Examiner further rejected claims 121-132, and 139-141 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that applicants had possession of the invention.

Specifically, the Examiner alleges that claims 121 and 139 recite "consisting essentially of 3-13 amino acids having at its carboxyl terminus the amino acid sequence (S/T)-X-(V/I/L)" as a limitation of the structure of a signal transducing protein which was not in the specification as originally filed.

In response, applicants respectfully traverse the Examiner's rejection. Applicants contend that the language "consisting essentially of 3-13 amino acids having at its carboxyl terminus the amino acid sequence (S/T)-X-(V/I/L)" has support in the specification as filed, *inter alia* at page 28, line 6 to page 30, line 15, detailing the identification of the amino acid sequence (S/T)-X-(V/I/L) and the minimal peptide stretch required for binding. In addition, as shown in Figure 3B, the required minimal peptide stretch may be composed of at least three amino acids, representing the carboxyl terminus amino acid sequence (S/T)-X-(V/I/L) alone, and up to fifteen amino acids. The same level of inhibitory effect on the binding of the signal transducing protein to the cytoplasmic protein was achieved with these peptides. Thus, the specification substantiates a peptide consisting essentially of 3-13 amino acids including the consensus sequence (S/T)-X-(V/I/L) and its role in signal transducing proteins.

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In view of these remarks, applicants maintain that claims 121-141 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Rejections Under 35 U.S.C. §102(e)

The Examiner rejected claims 121-132 and 139-141 under 35 U.S.C. §102(e), as allegedly anticipated by Reed et al (U.S. Patent No. 5,876,939).

Specifically, the Examiner alleges that claims 121-132 and 139-141 are interpreted as methods encompassing the Fas receptor, because the claims are drawn to a "cytoplasmic protein" consisting essentially of 3-13 amino acids having at its carboxyl terminus the amino acid sequence (S/T)-X-(V/I/L).

In response, applicants respectfully traverse the Examiner's rejection. Applicants direct the Examiner's attention to the language of claim 121 which states, in pertinent part, that the "*signal-transducing protein*" is a peptide consisting essentially of 3-13 amino acids having at its carboxyl terminus the amino acid sequence (S/T)-X-(V/I/L). Hence, the applicants note that the amino acid sequence (S/T)-X-(V/I/L) is used to describe the signal transducing protein, not the cytoplasmic protein as the Examiner alleges.

In addition, applicants note that the Reed Patent does not teach a peptide consisting essentially of 3-13 amino acid having the consensus sequence (S/T)-X-(V/I/L) disclosed in the subject application. Hence, the rejected claims are not anticipated, since Reed does not teach each and every element thereof.

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In view of these remarks, applicants maintain that claims 121-141 satisfy the requirements of 35 U.S.C. §102(e).

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the rejections, and earnestly solicit allowance of the pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

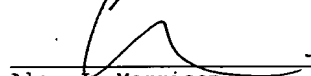
No fee, other than the enclosed \$55.00 for a one-month extension of time, is deemed necessary in connection with this Communication. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Assistant Commissioner for Patents,
Washington, D.C. 20231.


Alan J. Morrison
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- 12/13/02
Date